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| EXAMINER | |
|---|---|
| SALVOZA, M FRANCO G | |
| **ART UNIT** | **PAPER NUMBER** |
| 1648 | |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/822,613 | SCARPACE ET AL. | |
| | Examiner | Art Unit | |
| | M. Franco Salvoza | 1648 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *11 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *13-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 21-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/11/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Claim 22 has been amended.

Claims 1-12, 21-40 are under consideration.

### *Claim Objections*

### WITHDRAWN

Claim 22 was objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim.

In light of applicant's amendment the objection is withdrawn.

### *Claim Rejections - 35 USC § 103*

### MAINTAINED

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 4, 5, 6, 7, 10-12, 21-38, 40 were rejected under 35 U.S.C. 103(a) as being unpatentable over Pritchard et al. in view of Wilson et al. (WO/2000/28061)

Claims 1, 2, 4, 5, 6, 7-12, 21-38, 40 were rejected under 35 U.S.C. 103(a) as being unpatentable over Pritchard et al. and Wilson et al. in view of Lasic et al.

Claims 1, 2, 3, 4, 5, 6, 7, 10-12, 21-38, 39, 40 were rejected under 35 U.S.C. 103(a) as being unpatentable over Pritchard et al. and Wilson et al. in view of Paterna et al. ("Influence of

promoter and WHV post-transcriptional regulatory element on AAV-mediated transgene expression in the rat brain," Gene Therapy, 7, pp. 1304-1311 (2000)).

Applicant contends that there is neither the suggestion nor the reasonable expectation of success for combining the references; further that the combination of references fails to satisfy the *In re O'Farrell* tripartite test, including references containing detailed enabling methodology; no combination of the cited references provides sufficient evidence that the rAAV-POMC based constructs could be successfully used in providing therapeutic amounts of POMC polypeptides to a mammalian brain or for treating obesity via central POMC therapy; the rejections are merely an obvious to try situation; further, Pritchard and Wilson are not combinable because Pritchard does not mention the viral vector compositions, etc.; Lasic fails to provide the reasonable expectation of success because Lasic neither teaches nor suggests the use of rAAV vectors that express one or more nucleic acid segments encoding a POMC polypeptide; Paterna 2 does not teach use of promoters to alter the expression of a rAAV based gene construct encoding a biologically active POMC polypeptide.

Additionally, applicant included Exhibit A providing results that a rAAV-POMC vector to the brains of a mammalian model of obesity resulted in responses that lasted at least 45 days in one study and at least 80 days in another; thus the nature of the response could not have been predicted; applicant points to Mizuno et al. demonstrating weight reducing effect as a result of POMC overexpression in the transgenic mouse.

Applicant's arguments are considered but found unpersuasive.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the

teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). Further, the requisite test for obviousness is the *Graham v. John Deere* factors.

In this case, claim 1 recites a product of a composition comprising recombinant adeno-associated viral (rAAV) vector that comprises a nucleic acid segment encoding a pro-opiomelanocortin polypeptide operably linked to a promoter capable of expressing said segment in a host cell that comprises said vector, wherein said polypeptide activates the central melanocortin pathway in a mammal that expresses said vector.

The dependent claims recite activating the central melanocortin pathway; for diagnosing, preventing, treating or ameliorating the symptoms of a POMC deficiency condition in a mammal; formulated for administration to human brain; to the arcuate nucleus of a human hypothalamus; for intracerebroventricular administration; wherein said mammal has been diagnosed with obesity, adiposity, or suffers from excessive body weight gain; wherein said mammal has a POMC deficiency condition resulting in polyphagia, etc.

Still, the claims recite the product of a composition comprising recombinant adeno-associated viral (rAAV) vector that comprises a nucleic acid segment encoding a pro-opiomelanocortin polypeptide operably linked to a promoter capable of expressing said segment in a host cell that comprises said vector, wherein said polypeptide activates the central melanocortin pathway in a mammal that expresses said vector.

Wilson teaches rAAV vectors for gene therapy and the delivery and expression of "any" heterologous gene or "any" minigene or "any" nucleic acid sequence. (p. 9).

Pritchard et al. teaches POMC is an important means of controlling the central melanocortin system; POMC derived peptides play a central role in the regulation of food intake; (p. 760).

In regards to the claim limitations "formulated for administration to human brain; to the arcuate nucleus of a human hypothalamus; for intracerebroventricular administration," a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

The state of the art at the time indicates that it was known to those of ordinary skill in the art that the gene products of the POMC gene play an important role in controlling human energy balance. Dhillon et al. and Bagnasco et al. were cited in support. To cite further in support, Newell-Price ("Proopiomelanocortin gene expression and DNA methylation: implications for Cushing's syndrome and beyond," (April 2, 2003) teaches proopiomelanocortin gene expression and POMC peptides bind the melanocortin receptor in the arcuate nucleus, signaling satiety (p. 371); Jackson and O'Rahilly ("Letters to the Editor" (1998)) teach defects that affect the function or expression of POMC-derived ligands lead to human and murine obesity (p. 819).; Yaswen et al. ("Obesity in the mouse model of pro-opiomelanocortin deficiency responds to peripheral melanocortin" (1999)) teaches therapeutic use of peripheral melanocortin in the treatment of obesity (p. 1066); McMinn et al.; Zimanyi et al. ("The role of melanocortin peptides and

receptors in regularion of energy balance" (March, 2003) teaches that alpha-MSH, a 13 amino acid peptide secreted as a product of the pro-opiomelanocortin gene in the pituitary is a potent agonist of 4 of the 5 cloned melanocortin receptors (p. 627); MacNeil et al. ("The role of melanocortins in body weight regulation: opportunities for the treatment of obesity" (2002)) teaches "diverse lines of evidence, including genetic and pharmacological data obtained in rodents and humans, support a role for the melanocortin MC3 and MC4 receptors in the regulation of energy homeostasis (p. 93).

The references supported by weight of the state of the art at the time of invention provide the requisite ***motivation*** (emphasis added) and ***reasonable*** (emphasis added) expectation of success for the claimed invention. Notice that the claims do not claim "***successful use in providing therapeutic amounts*** of POMC polypeptides (emphasis added) to a mammalian brain or for treating obesity via central POMC therapy" (notice the term "treating" is encompasses mere administration of the vector); the claim recites the product of vector comprising a nucleic acid segment encoding a POMC peptide, wherein the peptide activates the melanocortin pathway for recited intended uses.

Further, Lasic et al. and Paterna et al. were not cited to teach every element of the claimed invention. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In regards to Applicant's submitted Exhibit A, the submission and results are noted, however, the nature and potency of the response are not recited in the claim, which recites the

product (which is obvious in light of the combined references and state of the art at the time for the reasons cited) of the recombinant adeno-associated viral (rAAV) vector that comprises a nucleic acid segment encoding a pro-opiomelanocortin polypeptide operably linked to a promoter capable of expressing said segment in a host cell that comprises said vector, wherein said polypeptide activates the central melanocortin pathway in a mammal that expresses said vector.

The rejections are maintained for reasons of record.

***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to M. Franco Salvoza whose telephone number is (571) 272-8410. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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